

REMARKS

Claims 1-3, 11-17, 19-20, 27, 29, 32 and 34-44 are pending and under consideration in the present application. Claims 34-45 remain withdrawn. Applicant is cancelling claims 6, 7, 8, 9, 10, 18, 23, 26, 28, 33 and 45. Applicant has amended claims 1, 17, 19, 20, and 27, and added new claims 46-54, but no new matter has been added.

Support for new claims 46-54 is found throughout the specification. *See, e.g.*, Pub. No. US2002/0182207, Paragraphs 0009, 0016, 0031, 0059, 0148, and Examples 1-5 (*e.g.*, Paragraphs 0138, 0142, 0148, 0150, 0156, 0177, 0194, 0213).

I. Specification Objection.

An objection to paragraph 0250 of the disclosure was made because it contains an embedded hyperlink and/or other form of browser-executable code. (Office Action, p. 2). Applicant has amended paragraph 0250 of the disclosure to remove the embedded hyperlink or other form of browser-executable code. Accordingly, the Examiner's objection is now moot.

Applicant respectfully requests that the Examiner withdraw the objection to paragraph 0250 of the Specification.

II. Section 112, Second Paragraph Rejection: Alleged Indefiniteness

Claims 17-20, 23, 26-29 and 32 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite. Claim 17 is rejected because it is directed to "any non-naturally occurring enzyme." (Office Action, p. 2). Applicant has amended claim 17 to refer to a catalytic antibody rather than a "non-naturally occurring enzyme." Applicant has also amended dependent claims 19 and 20 to refer to the catalytic antibody rather than to the enzyme of claim 17. Applicant has canceled claims 18, 23, 26, and 28. Therefore, these rejections are now moot.

Additionally, although claims 27-29 and 32 are also rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite, the only basis for that rejection cited in the Office

Action is claim 17's reference to a "non-naturally occurring enzyme." (Office Action, p. 2). Since claims 27-29 and 32 do not refer to a "non-naturally occurring enzyme," the rejection is clearly not applicable to those claims.

Accordingly, favorable reconsideration and withdrawal of the Section 112, second paragraph, rejection is respectfully requested.

III. Section 112, First Paragraph Rejection: Alleged Lack of Written Description

Claims 1-3, 6, 10-20, 23, 26-29 and 32 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in a way that conveys that the inventor(s) had possession of the claimed invention as of the filing date. (Office Action, pp. 3-4). The Examiner argues that the specification: (1) fails to describe "non-naturally occurring enzymes" with respect to claims 17-20, 23 and 26 (*id.* at pp. 3 and 9); (2) insufficiently describes representative species encompassed by the genus of the claim with regard to claims 1-3, 10-12, 17-20, 23, 26-29 and 32 (*id.* at pp. 4-7); (3) lacks any structure-function correlation with regard to the "members of the genus of target molecules and their functional groups capable of forming a bond with a function group on the label" or with regard to the members of the genus of enzyme molecule recited in claims 17-20, 23, 26-29 and 32 (*id.* at p. 7); and (4) only teaches an example "wherein an antibody attaches a label to target molecule," which is "not representative of the entire genus that the instant claims recite" (i.e., "methods of modifying any biological molecules by attaching any label using any catalytic antibody via formation of any bond between said target molecule and label") (*id.* at pp. 8-9).

Applicant respectfully submits that the amendments to independent claims 1, 17 and 27 and dependent claims 19 and 20 render the written description rejections moot. Applicant has amended independent claim 17 to replace a "non-naturally occurring enzyme" with a "catalytic antibody" and dependent claims 19 and 20 to replace "enzyme" with "catalytic antibody."

Support for these amendments is found throughout the specification (*see, e.g.*, Pub. No. US2002/0182207, Paragraphs 0009-0010, 0016, 0018, 0027-0028; Examples 2-5). Independent claims 1, 17 and 27 have been amended to indicate that the catalytic antibody is capable of chemically modifying a biologically active target molecule by attaching a label to the target molecule “by glycosylation or acylation.” Support for these amendments is found in the specification of Pub. No. US 2002/0182207 at Paragraphs 0009, 0016, and Examples 2-5. Independent claims 1, 17 and 27 have been amended to indicate that the target molecule is selected from the group consisting of “TNF α , IL-4, IL-6, and VEGFr2.” Support for these amendments is found throughout the specification (*see, e.g.*, Pub. No. US2002/0182207, Paragraphs 00009, 0011, 0016, 0018, 0019, 0066-0085; Examples 2-5). Finally, independent claims 1, 17, and 27 have been amended to indicate that the label is “selected from the group consisting of a sugar and a β -lactam antibiotic.” Support for these amendments is found, for example, in the specification of Pub. No. US2002/0182207 at Paragraphs 0009, 0016, 0031, 0148 and Example 2.

An applicant shows possession of an invention “by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention.” *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997). “Possession may be shown in a variety of ways including description of an actual reduction to practice, or by showing that the invention was “ready for patenting” such as by the disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention. *See, e.g., Pfaff v. Wells Electronics, Inc.*, 525 U.S. 55, 68, 119 S.Ct. 304, 312, 48 USPQ2d 1641, 1647 (1998); *Reagents of the University of California v. Eli Lilly*, 119 F.3d 1559, 1568, 43

USPQ2d 1398, 1406 (Fed. Cir. 1997); *Amgen, Inc. v. Chugai Pharmaceutical*, 927 F.2d 1200, 1206, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991) (one must define a compound by “whatever characteristics sufficiently distinguish it”).” (MPEP § 2163(I)).

Applicant submits that the claimed method and compositions are described in the specification as discussed above in sufficient detail to satisfy the requirements of the first paragraph of 35 U.S.C. § 112. (See MPEP § 2163.02, “Standard for Determining Compliance with the Written Description Requirement”). When one considers the high degree of skill in the art, one will readily appreciate that the Applicant has provided sufficient details regarding the catalytic antibody, the target molecule, the label, the bond formation and the remaining elements and defining characteristics of the claimed invention to distinguish the invention.

“In claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate description of the claimed genus.” *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406; MPEP § 2163 (III-3(a)), page 2100-179, left-hand column). Still further, MPEP § 2163 (III-3(a)) clearly states that “although structural formulas provide a convenient method of demonstrating possession of specific molecules, other identifying characteristics or combinations of characteristics may demonstrate the requisite possession.” As explained by the Federal Circuit, “there is no per se rule that an adequate written description of an invention that involves a biological macromolecule must contain a recitation of known structure.” *Falkner v. Inglis*, 448 F.3d 1357, 1366, 79 USPQ2d 1001, 1007 (Fed. Cir. 2006). See also *Capon v. Eshhar*, 418 F.3d 1349, 1358, 76 USPQ2d 1078, 1084 (“The Board erred in holding that the specifications do not meet the written description requirement because they do not reiterate the structure or formula or chemical name for the nucleotide

sequences of the claimed chimeric genes" where the genes were novel combinations of known DNA segments.). For example, a disclosure of unique cleavage by particular enzymes, isoelectric points of fragments, detailed restriction enzyme maps, a comparison of enzymatic activities, or antibody cross-reactivity may be sufficient to show possession of the claimed invention to one of skill in the art. *See Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966 ("written description" requirement may be satisfied by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that fully set forth the claimed invention"). (MPEP § 2163-III-3(a)).

Applicant respectfully submits that it is improper to reject claims on the ground that the specification does not support the claims when the terms of the claim are no broader than the broadest description of the invention in the specification and there is no reason to challenge the operativeness of the subject matter embraced by the claims. *Ex parte Altermatt*, 183 USPQ 436 (POBA 1974).

Thus, one of ordinary skill in the art would readily recognize from the original disclosure that Applicant invented the presently claimed subject matter. Applicant submits that the Examiner's allegation that the specification is deficient in that it does not show working examples is not relevant to a determination of whether Applicant has satisfied the written description requirement of the first paragraph of 35 U.S.C. § 112.

Applicant believes that the amendments to independent claims 1, 17 and 27 and dependent claims 19 and 20 render the written description rejection moot, and, therefore, respectfully requests that this rejection be withdrawn.

IV. Rejection Under Section 112, First Paragraph: Alleged Lack of Enablement

Claims 1-3, 6, 10-20, 23, 26-29 and 32 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly non-enabled. The Examiner alleges that the specification does not enable

the skilled artisan to make and use the claimed invention because “[t]hese claims are so broad to encompass any enzyme or catalytic antibody molecule capable of catalyzing formation of any bond between any function group of any biological target molecule or any TNF α , IL-4, IL-6 or VEGFr2 type target molecule and any functional group of any label or any beta-lactam antibiotic type label molecule and methods of modifying any biological molecule by attaching said label using said catalytic antibody.” (Office Action, pp. 10-11).

Applicant respectfully submits that the amendments to independent claims 1, 17 and 27 and dependent claims 19 and 20 render the enablement rejection moot. Applicant has amended independent claim 17 to replace a “non-naturally occurring enzyme” with a “catalytic antibody” and dependent claims 19 and 20 to replace “enzyme” with “catalytic antibody.” Independent claims 1, 17 and 27 have been amended to indicate that: (1) the catalytic antibody is capable of chemically modifying a biologically active target molecule by attaching a label to the target molecule “by glycosylation or acylation”; (2) the target molecule is selected from the group consisting of “TNF α , IL-4, IL-6, and VEGFr2”; and (3) the label is “selected from the group consisting of a sugar and a β -lactam antibiotic.” Examples 1-5 provide the detail, direction and guidance for generating the catalytic antibodies according to the amended claims.

As discussed in the previous Amendment and Response To office Action, MPEP § 2164.01 (a) enumerates a number of factors for determining whether experimentation is undue. The Applicant asserts that considering all of these factors the experimentation inherent in antibody generation and in the generation of antibodies according to the invention is not undue. In the instant specification there is considerable detail, direction and guidance, for generating antibodies as claimed. When the disclosure is given careful consideration by a skilled artisan, it would be apparent that the quantity of experimentation required to reduce the invention to practice is not undue.

Enablement is not precluded by the necessity for some experimentation such as routine screening. Instead, experimentation needed to practice the invention must not be undue experimentation. The key word is “undue” not “experimentation.” “The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed.” *See, e.g.*, MPEP § 2164.06. “The test for enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation.” A patent may be enabling even though some experimentation is necessary. *United States v. Teletronics, Inc.* 857 F.2d 778, 8 USPQ2d 1217 (Fed. Cir. 1988), *cert. denied*, 490 U.S. 1046 (1989).

The generation of antibodies such as those used in the claimed methods, like the generation of conventional antibodies requires a certain amount of experimentation to screen for antibodies with the appropriate activity and may not always be successful. In *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988), the Federal Circuit held that such experimentation, when carried out for generation of conventional monoclonal antibodies, is reasonable and not undue because of the high level of skill in the pertinent art and, also, because of the considerable direction and guidance provided in the specification on how to practice the invention.

Moreover, working examples are not required to satisfy the enablement requirement. (MPEP § 2164.02). Although the Examiner may prefer working examples, the preference does provide a substitute for current legal standards of patentability. The specification provides extensive disclosure of the methods of making and using catalytic antibodies, as well as target molecules to be modified by disclosed antibodies. Every stage of the process is disclosed in great detail, thus enabling a person of ordinary skill in the art to practice the claimed invention

without undue experimentation. The disclosure also teaches how to test the antibodies for the desired activity, e.g., catalytic antibody can be identified by screening human phage antibody display libraries against an antibiotic-target conjugate. The specification teaches selecting labels that exhibit a low but detectable reaction with the desired target in the absence of a catalyst, for example, the conjugation reaction of β -lactam antibiotics with proteins (Pub. No. US2002/0182207, Paragraph 0032). The same passage in the specification also notes that the fact that the uncatalyzed reaction can occur at a slow rate places a lower burden on the catalyst and may only require that the catalyst bind to both the target and label so as to hold them in close proximity and increase their effective concentrations. (*Id.* at Paragraph 0033). In addition, the specification is not limited to selection of catalytic antibodies by panning phages and also teaches a variety of other approaches including directed evolution under selective pressure and/or the mutation of catalysts with similar chemical activities but different structural specificity. The fact that the specification does not provide working examples of the elicitation of catalytic antibodies does not support the Examiner's rejection. *See Atlas Powder Co. V. E.I. Du Pont De Nemours & Co.*, 224 USPQ 409, 414 (Fed. Cir. 1984). That is especially true here where Applicant's feasibility studies demonstrated that antibodies could be preselected by phage display (Example 1) and Applicant disclosed in detailed prophetic examples the production of catalytic antibodies using TNF α , VEGFr2, IL-4 and IL-6 as the target molecule (Examples 2-5).

Contrary to the Examiner's suggestion, the specification need not provide examples or specific description of embodiments for the entire scope of the invention. Detailed procedures for making and using an invention may not be necessary if the description of the invention itself is sufficient to permit those skilled in the art to make and use the invention. (MPEP § 2164). "A patent does not teach, **and preferably omits**, what is well known in the art. *In re Buchner*, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991); *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 231 USPQ

81, 94 (Fed. Cir. 1986), *cert. denied*, 480 U.S. 947 (1987); *Lindemann Maschinenfabrik GMBH v. American Hoist & Derrick Co.*, 730 F.2d 1452, 1463, 221 USPQ 481, 489 (Fed. Cir. 1984).” (MPEP § 2164.01, emphasis added).

Moreover, the Applicant has previously submitted evidence regarding the advanced level of skill in the relevant art (*see* Applicant’s arguments regarding Nevinsky et al., and Stevenson et al.).

Applicant asserts that the amended claims are fully enabled by the disclosure and further in view of the high state of relevant art. Favorable consideration of the amended claims is earnestly solicited.

V. Rejection Under 35 U.S.C. § 102(b): Alleged Anticipation

A. Alleged Anticipation by Tanaka et al.

Claims 17-20, 23, 26-29 and 32 are rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Tanaka et al. (Tet. Lett. (1999): 8063-66) (“Tanaka”). The Examiner continues to contend that Tanaka teaches a catalytic antibody that assists in the formation of an acyl-enzyme bond between beta-lactamase (as the alleged target) and a β -lactam-type compound (as the label). (Office Action, p. 16).

Applicant respectfully disagrees that Tanaka anticipates the claims. A claim is anticipated only if each and every element of the claim is found, either expressly or inherently, in a single prior art reference. *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631 (Fed. Cir. 1987). The instant amended claims are directed to selecting a target molecule from the group consisting of TNF α , IL-4, IL-6, and VEGFr2. Tanaka et al. does not teach any of these target molecules. Accordingly, withdrawal of the Section 102 anticipation rejection based on Tanaka is respectfully requested.

B. Alleged Anticipation by Nardone et al.

Claims 17-20, 23, 26-29 and 32 are rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Nardone et al. (J. Biol. Chem. (1986) Vol. 261: 12128-33) (“Nardone”). The Examiner contends that Nardone “teaches BamHI endonuclease and methylase wherein the methylase methylates cytosine of a DNA molecule and in doing so modulates the DNA molecule so that it is resistant to cleavage by endonuclease.” (Office Action, p. 17).

Applicant respectfully disagrees that Nardone anticipates the claims. A claim is anticipated only if each and every element of the claim is found, either expressly or inherently, in a single prior art reference. *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631 (Fed. Cir. 1987). The instant amended claims are directed to “a catalytic antibody” or “a composition comprising a catalytic antibody” and to a target molecule selected from the group consisting of TNF α , IL-4, IL-6, and VEGFr2. Nardone does not teach a catalytic antibody nor does it teach any of these target molecules. Accordingly, withdrawal of the Section 102 anticipation rejection based on Nardone is respectfully requested.

CONCLUSION

In view of the foregoing amendments and remarks, reconsideration of Claims 1-3, 11-17, 19-20, 27, 29, 32, 34-44, and new claims 46-54 pending in this application and allowance are earnestly solicited.

No additional fees are believed due except for the fee for a two-month extension of time. However, the Commissioner is hereby authorized to charge any required fees and credit any overpayments to **Deposit Account No. 50-0540**.

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Respectfully submitted,

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